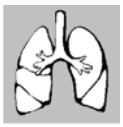
CDHS/CTCA JOINT GUIDELINES
Targeted Skin Testing and Treatment of Latent Tuberculosis Infection in Adults and Children



The following guidelines have been developed by the California Department of Health Services, Tuberculosis Control Branch in consultation with the Executive Committee of the California Tuberculosis Controllers Association. These guidelines are official State recommendations and have been endorsed by the California Tuberculosis Controllers Association.

Recently published guidelines from the American Thoracic Society and Centers for Disease Control and Prevention have recommended a change in nomenclature. The terms "chemoprophylaxis" and "preventive therapy" will no longer be used. Instead, the phrase "treatment of latent tuberculosis infection (LTBI)" is recommended because it more accurately describes the intended intervention. This change in nomenclature will hopefully promote greater understanding of the concept for both patients and providers, resulting in more widespread use of this important tuberculosis (TB) control strategy.

Targeted TB Skin Testing

Targeted tuberculin skin testing for LTBI aims to identify individuals at high risk for TB who would benefit from treatment of LTBI. Skin testing low risk populations will result in unnecessary testing and treatment because of false-positive test results.

High risk can be defined as:

(1) Recent infection with *Mycobacterium tuberculosis*,
(2) The presence of clinical conditions that are associated with an increased risk of progression of LTBI to active TB (see **Appendix 1: Tables 1 and 2**) or
(3) Increased morbidity if progression to TB disease occurs.

Definition of a positive tuberculin skin test

Previous vaccination with BCG is not a contraindication to tuberculin skin testing. Because most persons who have received prior BCG vaccination are from high prevalence areas of the world, previous vaccination should be ignored when interpreting a tuberculin skin test.

I. $\geq$ 5 mm of induration*

A. Persons known or suspected to have HIV infection.

B. Recent contacts to an active case of pulmonary or laryngeal TB.

C. Persons with an abnormal chest radiograph consistent with TB disease.

D. Immunosuppressed individuals (See page 4 **Indications for Treatment of LTBI -TB2 and TB4**, VI-E)

***Note:** The California Department of Corrections considers all inmates high risk, and therefore treats for latent infection all inmates with TST of $\geq$ 5mm.

II. $\geq$ 10 mm of induration

All persons except those in I (A) above

> **Note:** The CDC recommends using a 15 mm cutoff for low risk reactors. However, in California, public health departments do not recognize this cutoff because California is a high incidence state and the prevalence of nontuberculous mycobacterial infections is lower than other regions of the United States.

III. Tuberculin skin test conversion

TST conversion is defined as an increase of at least 10 mm of induration from < 10 mm to $\geq$ 10 mm within two years from a documented negative to positive TST.

Example: a TST of 4 mm that increases in size to 14 mm or more in induration would be considered a skin test conversion.

In some cases, the exact size (in mm) of the previous tuberculin skin test may not be known. In such cases, skin test conversion is defined as a change from a negative to positive tuberculin skin test within a 2-year period.

Evaluation for TB Disease - Symptom review and chest radiography

I. All persons who have a positive tuberculin skin test should undergo symptom review and have a chest radiograph.

A. If the radiograph is normal and the patient is asymptomatic, treatment of LTBI may be indicated (see **Appendix 2**).

B. If the radiograph is normal but the patient has a clinical presentation consistent with tuberculosis, further work-up is indicated and treatment of LTBI should be delayed until active tuberculosis has been ruled out.

II. Bacteriologic studies should be obtained for all persons with an abnormal chest radiograph consistent with tuberculosis even when the radiographic abnormalities appear stable. If bacteriologic studies are obtained, treatment of LTBI should not be initiated until final culture results are available.

Definition of persons eligible for treatment of LTBI (TB2 and TB4)

The following classes of persons are eligible for treatment of LTBI if they have not received a prior course of treatment for active TB or LTBI. In some cases, individuals may require another course of therapy. Indications for re-treatment include persons with a new close contact to an infectious case who are < 5 years of age, or have HIV/AIDS or other significant immunosuppression. Providers may also choose to retreat persons with previously treated LTBI or active TB who have had new exposure to a highly infectious TB case where extensive transmission has been documented, circumstances suggest a high probability of transmission, or in high risk settings such as prisons or other congregate facilities.

I. TB2 - Tuberculosis infection, no disease:

Significant reaction to tuberculin skin test, negative bacteriologic studies (if done) and no clinical and/or radiographic evidence of tuberculosis. Patients with isolated calcified granulomas or apical pleural thickening are generally classified as TB 2.

II. TB4 - Tuberculosis, no current disease:

A. History of previous episode(s) of tuberculosis, or

B. Abnormal*, but stable, radiographic findings in a person with a positive tuberculin skin test, negative bacteriologic studies, and no clinical and/or radiographic evidence of current disease.

*Abnormal refers to radiographs with parenchymal abnormalities consistent with TB, except isolated calcified granulomas.

Indications for Treatment of LTBI – TB2 and TB4 (See **Appendix 2**)

Persons in the following categories should be considered for therapy if their tuberculin skin test is positive and they have not previously completed a course of therapy for tuberculosis or LTBI.

I. Persons known or suspected to have HIV infection, regardless of age, including pregnant women.

II. Persons with an abnormal chest radiograph suggestive of tuberculosis and classified as a TB 4, regardless of age.

III. Recent close contacts to active pulmonary or laryngeal TB, regardless of age, including pregnant women.

IV. Tuberculin skin test converters within 2 years, regardless of age, including pregnant women.

V. Persons from countries with high TB rates

A. Recent arrivals (arrived within the past 5 years or less), regardless of age.

B. Remote arrivals (arrived over 5 years ago)

The CDC guidelines no longer recommend using a 35 year-old cutoff in deciding which individuals with LTBI should be treated. In California, where the majority of the TB cases occur in persons born outside of the United States, it is recommended that individuals who arrived over 5 years ago should still receive treatment for LTBI if they have a positive tuberculin skin test. Because the risk of INH-induced hepatitis is greater in older individuals, an age cutoff may be appropriate for this group. Local epidemiologic circumstances and resources should determine whether a specific age cutoff is warranted.

VI. Persons with the following conditions that have been associated with an increased risk of TB (See **Appendix 1, Tables 1 and 2**), regardless of age:

A. Injection drug use, regardless of HIV serostatus

B. Diabetes mellitus (especially insulin-dependent)

C. Silicosis

D. End-stage renal disease

E. Chronic immunosuppression

1. Transplant recipients
2. Prolonged corticosteroid therapy (≥15 mg/day for ≥ 1mo)
3. Other immunosuppressive therapy

F. Hematological and reticuloendothelial diseases

G. Malnutrition and clinical situations associated with rapid weight loss

1. Cancer of the head and neck
2. Intestinal bypass or gastrectomy
3. Chronic malabsorption
4. Low body weight (>10% below ideal body weight)

VII. Children and adolescents < 18 years of age exposed to adults with the above high risk characteristics.

VIII. Residents and employees of the following high risk congregate settings: prison and jails, nursing homes, and other long-term facilities for the elderly, residential facilities for patients with AIDS, and homeless shelters; other homeless persons; employees of hospitals and other health care facilities. In some jurisdictions, local epidemiology and limited resources may necessitate the use of an age cutoff for some populations.

IX. Persons with a positive tuberculin skin test who are not in the above categories.

Local epidemiologic circumstances and resources may define some populations such as persons abusing substances other than injection drugs (e.g. alcoholics and crack cocaine users) or other groups at risk for TB infection for whom treatment is indicated. There may be some of these populations for which an age cutoff is appropriate.

Indications for Treatment of LTBI – TB1 (See **Appendix 2**)

Close Contacts

In close contacts to infectious cases, the initial tuberculin skin test may be negative despite underlying infection with *M. tuberculosis* if the TST is placed before the contact has mounted an immune response to the tuberculin antigen. It takes 2-12 weeks after infection with *M. tuberculosis* to develop a positive TST reaction.

Close contacts (TB1) to an infectious case, who have a tuberculin skin test < 5 mm, should have a chest radiograph obtained, and once TB disease is excluded, should be started on therapy for LTBI regardless of age if (See CDHS/CTCA, "Contact Investigation Guidelines."):

I. Circumstances suggest a high probability of infection. For example, evaluation of other contacts

with a similar degree of exposure demonstrates a high prevalence of infection, documented converters, or secondary cases.

II. The contact is a child under 5 years of age, or is infected with HIV, or is otherwise immune-compromised.

For those individuals who are started on therapy with a TST < 5 mm, a repeat tuberculin skin test should be performed 10 to 12 weeks after contact with the infectious case has been broken, or the index case becomes non-infectious, to determine if the skin test has become positive. Decision on continuing therapy should be made once the result of repeat skin testing is available.

Note: In HIV infected contacts, treatment should be completed, regardless of the result of the repeat skin test.

Treatment Regimens (See **Appendix 3,** for drug dosages)

I. INH alone:

A. 6-9 months for immune-competent adults. While a 9-month regimen may provide a greater degree of protection, individual programs may choose to give 6 months of INH due to operational considerations (e.g., resources, adherence issues, etc.)

B. 9 month regimen for children and adolescents (up to age 16 - 18).

C. 9 month regimen for HIV-infected persons or persons suspected of having HIV infection

D. 9 month regimen for TB 4 (See also **below,** IV)

II. RIF and PZA for 2 months. This option may be preferred when longer therapy may not be feasible, (such as for jail inmates or homeless patients) and when the patient can be monitored closely. It may also be useful in persons exposed to INH resistant, RIF sensitive TB cases, when the individual is INH intolerant, or in HIV infected individuals for whom clinical trials have demonstrated the regimen's efficacy. RIF-PZA is not recommended for persons with underlying liver disease or for those who have had INH-associated liver injury. The 2-month RIF-PZA treatment regimen for LTBI should be used with caution, especially in patients concurrently taking other medications associated with liver injury, and those with alcoholism, even if alcohol use is discontinued during treatment. This regimen is not included in the list of accepted regimens of treatment for LTBI in children under the age of 18.

III. Rifampin alone for 4-6 months. This regimen has not been studied in randomized trials so it should be reserved for those individuals who cannot tolerate INH or PZA. For persons exposed to cases with mono-resistance to INH, the 2-month regimen of RIF and PZA is recommended. For persons who cannot tolerate PZA, a 4-6 month regimen of rifampin may be used.

IV. INH and RIF for 4 months for TB 4. Although there have been no randomized studies to document the efficacy of this regimen in persons classified as TB 4, there is a great deal of experience with this regimen in the public health sector.

V. Rifabutin may be substituted for rifampin in the above regimens in situations where rifampin cannot be given such as in HIV-infected persons taking certain protease inhibitors or non-nucleoside reverse transcriptase inhibitors. Dosage adjustments may, however, be necessary. An expert should be consulted.

VI. Regimens for Contacts to Drug Resistant Cases

A. INH mono-resistant source case

For contacts to cases of INH mono-resistance, the 2-month regimen of RIF and PZA is recommended. For persons who cannot tolerate PZA, a 4-6 month regimen of rifampin may be used.

B. Multidrug resistant source case

PZA and EMB, or PZA and a flouroquinolone for 6-12 months for high risk contacts, e.g. immune-compromised persons exposed to MDR-TB cases. These regimens should be given only after TB disease has been ruled out and provided that the organism isolated from the source case is susceptible to PZA, EMB or flouroquinolones. An expert should be consulted.

Daily vs. Intermittent Dosing

Both INH and RIF/PZA regimens may be given daily or intermittently. Although the daily RIF/PZA regimen is preferred over the intermittent regimen, individual programs may choose to give the intermittent regimen for operational considerations (e.g., resources, adherence issues, etc.). When the RIF/PZA regimen is given intermittently, the current recommendation is to consider a 3-month duration of therapy. *When any of the above regimens are given intermittently, they must be administered as directly observed therapy (DOT), only.*

Directly Observed Therapy

Directly observed therapy (DOT) for LTBI should be used in circumstances where the risk of non-adherence is judged to be high or when the treatment regimens are given intermittently. New short course regimens and intermittent dosing may make DOT more feasible.

Monitoring for Drug Toxicity and Adherence

I. Baseline Evaluation

A. All patients taking RIF-PZA should have a serum transaminase (AST or ALT) and bilirubin at baseline. With the other regimens for LTBI, baseline laboratory testing is not routinely indicated, even for those over 35 years of age. Such testing may, however, be considered on an individual basis. Persons with the following high-risk characteristics should have baseline laboratory testing:

1. HIV infection
2. History of, or at risk of, chronic liver disease
3. Alcoholism
4. Taking other hepatotoxic medications

Note: Some experts recommend that pregnant women and those in the immediate post-partum period (within 3 months of delivery) have baseline liver function tests measured, also.

B. The baseline laboratory tests will depend on which drug regimen is being used.

1. Isoniazid-containing regimen –If baseline laboratory tests are indicated, a serum AST or ALT and bilirubin should be included.
2. Rifampin (or rifabutin) -containing regimen – In persons taking a rifamycin, baseline measurements of complete blood count and platelets are recommended, in addition to liver function tests.
3. Pyrazinamide-containing regimen – same as rifampin-containing regimen. A baseline uric acid level is not necessary unless the patient has a history of gout.

II. Evaluation During Treatment

A. Clinical Evaluation – Patients being treated for LTBI should receive a clinical evaluation at least monthly, regardless of the regimen used. The evaluation should include careful in person questioning of the patient about side effects associated with the medications, particularly hepatitis (e.g., anorexia, malaise, abdominal pain, fever, nausea, vomiting, dark urine, icterus). In addition, the patient should be asked about adherence and educated about the possible side-effects of the medications.

B. Rifampin and pyrazinamide containing regimens require more frequent monitoring. The CDC recommends that patients taking a rifampin-pyrazinamide regimen be reassessed in person by a health care provider at weeks 2, 4, 6 and 8 of therapy

At each visit, health care providers conversant in the patient's language (or with an appropriate interpreter) should instruct patients to stop taking RIF-PZA immediately and seek medical consultation if anorexia, nausea, abdominal pain, emesis, jaundice, or other hepatitis symptoms develop. Provider continuity is recommended for monitoring. No more than a 2-weeks supply of RIF-PZA (with a PZA dose of 15-20 mg/kg/d and a maximum of 2 gm/d) should be dispensed at a time to facilitate periodic clinical assessments.

A serum AST or ALT and bilirubin should be measured at baseline and at 2, 4, and 6 weeks of treatment in patients taking RIF-PZA. Because some side effects may occur in the second month of treatment, patients should be monitored throughout the entire course of treatment. Asymptomatic serum AST or ALT increases are expected and usually do not require that treatment be stopped. However, treatment should be stopped and not resumed for any of these findings:

- AST or ALT greater than five times the upper limit of normal range in asymptomatic persons
- AST or ALT greater than normal range when accompanied by symptoms of hepatitis
- Serum bilirubin greater than normal range.

C. For regimens other than RIF-PZA, routine laboratory monitoring during treatment of LTBI is indicated for those whose baseline liver function tests are abnormal, for persons at high risk of hepatic disease, or persons with symptoms of hepatitis. The frequency of this monitoring will vary depending on the person's risk of liver disease and the severity of the liver function test abnormalities.

> **Note**: Some experts recommend that pregnant women and those in the immediate post-partum period (within 3 months of delivery) have repeat liver function tests measured, also.

Medications should be stopped if the transaminase levels exceed 3-4 times the upper limit of normal if associated with symptoms and 4-5 times the upper limit of normal if the patient is asymptomatic. Medication should be held pending clinical laboratory results.

> **Note:** Any cases of severe liver injury (leading to hospitalization or death) in persons receiving any regimen for LTBI should be reported to the Surveillance and Epidemiology Section of the California Department of Health Services, TB Control Branch at (510) 540-2973, and will be forwarded to the Centers for Disease Control.

Completion of Therapy

Completion of therapy should be based on the total number of doses administered–not on duration of therapy. If treatment is interrupted the recommended number of doses of the regimen should be provided within a certain maximum time period (See **Appendix 3**). The entire regimen should be restarted if interruptions were frequent or prolonged enough to preclude completion of doses in the time frames specified. When therapy is restarted after an interruption of more than 2 months, a medical examination to exclude active disease is indicated.

> **Note:** No set of guidelines can cover all individual treatment situations that can and will arise. Thus, when questions on individual situations not covered by these guidelines do arise, consult with the Local TB Control Program, the California Department of Health Services, TB Control Branch, or the Tuberculosis Warmline, for further information.

Suggested Readings

1. American Academy of Pediatrics. 2000. Tuberculosis. *In* Red Book: Report of the Committee on Infectious Diseases, 25th ed. American Academy of Pediatrics, Elk Grove Village IL.

2. American Thoracic Society / Centers for Disease Control and Prevention. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994; 149: 1359-1374.

3. American Thoracic Society / Centers for Disease Control and Prevention. Targeted skin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med. 2000 161: S221-S247.

4. American Thoracic Society / Centers for Disease Control and Prevention. Diagnostic standards and classification of tuberculosis in adults and children. Am J Respir Crit Care Med 2000;161:1376-1395.

5. Centers for Disease Control and Prevention. Notice to readers. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. MMWR 2000;49:185-189.

6. Centers of Disease Control and Prevention. Update. Fatal and Severe Liver Injuries Associated with Rifampin and Pyrazinamide for Latent Tuberculosis Infection and Revisions in American Thoracic Society/CDC Recommendations – United States, 2001. MMWR 2001; 50.

7 Zuber PLF, McKenna MT, Binkin NJ, Onorato IM, Castro KG. Long-term risk of tuberculosis among foreign-born persons in the United States. J.A.M.A. 1997;278:304-307.

Appendix 1

High Risk Populations

Table 1. Incidence of Active TB in Persons with a Positive TST by Selected Factors

Risk Factor	TB Cases/1000 person-years
Infection > 2 years past	**1.6**
Infection < 1 year past	**12.9**
HIV Infection	**35.0-162.0**
Injection Drug Use	
HIV seropositive	**76.0**
HIV seronegative or unknown	**10.0**
Silicosis	**68**
Radiographic findings consistent with old TB	**2.0-13.6**

Source: American Thoracic Society/Centers for Disease Control and Prevention, 2000

Table 2. Certain medical conditions associated with an increased risk of developing TB

Medical Condition	Relative Risk
Solid organ transplant	
Renal	**37**
Cardiac	**20-74**
Jejunoileal bypass	**27-63**
Silicosis	**30**
Chronic Renal Failure/Hemodialysis	**10.0-25.3**
Carcinoma of head and neck	**16**
Gastrectomy	**2-5**
Diabetes mellitus	**2.0-4.1**

Source: American Thoracic Society/Centers for Disease Control and Prevention, 2000

Appendix 2

CANDIDATES FOR TREATMENT OF LATENT TUBERCULOSIS INFECTION (LTBI) (adapted from Charles P. Felton National TB Center)			
Category of person tested	TST <5 mm	TST ≥5 mm	TST ≥10 mm
(A) Recent Contact to TB Case [1]{tc "Recent Contact to TB Case [1]"}			
1. Child <5 years and recent contact[2]	TREAT	TREAT	TREAT
2. HIV-infected and recent contact[2]	TREAT	TREAT	TREAT
3. Immunosuppressed and recent contact[2]	TREAT	TREAT	TREAT
4. Other recent contact of TB case	Do Not Treat	TREAT	TREAT
(B) No Recent Contact to TB Case**{tc "**No Recent Contact to TB Case**"}**			
1. Fibrotic changes on chest X-ray[3]	Do Not Treat	TREAT	TREAT
2. HIV-infected	Do Not Treat	TREAT	TREAT
3. Injection drug user with unknown HIV status	Do Not Treat	TREAT	TREAT
4. Other immunosuppressed persons[4]	Do Not Treat	TREAT	TREAT
5. Recent skin test converters within 2 years	Do not Treat	Do Not Treat	TREAT
6. Foreign-born persons from endemic country[5]	Do Not Treat	Do Not Treat	TREAT
7. Injection drug user known to be HIV negative	Do Not Treat	Do Not Treat	TREAT
8. Resident/Employee institutional setting[6]	Do Not Treat	Do Not Treat	TREAT
9. Mycobacteria lab personnel	Do Not Treat	Do Not Treat	TREAT
10. High-Risk clinical conditions[7]	Do Not Treat	Do Not Treat	TREAT
11. Children < 18 years of age exposed to adults at high risk	Do Not Treat	Do Not Treat	TREAT
12. Other persons depending on local epidemiology and resources	Do Not Treat	Do Not Treat	TREAT

Note: If a person meets more than one criteria for treatment, the lower TST cut point for therapy should be used (i.e. an immigrant from a TB endemic country who has fibrotic changes on chest radiograph should be treated if the TST is ≥ 5 mm induration)

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[11]Recent contacts to active case of pulmonary or laryngeal TB.

[2]Recent contacts who are initially TST-negative should have a TST repeated 8-12 weeks after last exposure to TB case (see Text). Treatment can usually be discontinued after negative second TST in children. HIV infected adults and children, however, should receive full course of therapy regardless of TST result.

[3]Abnormal, stable, radiographic findings (parenchymal abnormalities consistent with TB, not isolated calcified granuloma or apical pleural thickening). Bacteriologic studies should be obtained for all persons with an abnormal chest radiograph consistent with TB even when the radiographic abnormalities appear stable. When bacteriologic studies are obtained, treatment of LTBI should not be initiated until final culture results are available.

[4]Transplant recipients, prolonged corticosteroid therapy (≥15 mg/day for ≥1 month), other immunosuppressive therapy

[5]Local epidemiologic circumstances and resources should determine whether a specific age cutoff is warranted in persons who have resided in the U.S. for over 5 years.

[6]Residents and employees of the following high risk congregate settings: prisons and jails*, nursing homes and other long-term facilities for the elderly, residential facilities for patients with AIDS, homeless shelters; other homeless persons; employees of hospitals and health care facilities.

*The California Department of Corrections considers all inmates high risk, and therefore treats for latent infection all inmates ≥ 5mm.

[7]Silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g. leukemias and lymphomas), other specific malignancies (e.g. carcinoma of the head and neck or lung), weight loss of ≥ 10% of ideal body weight, gastrectomy, jejunoileal bypass.

Pregnancy: Treat during pregnancy if either HIV-infected or recent *M.tb* infection.

Appendix 3

Recommended Drug Treatment Regimens For Treatment of LTBI

Drug	Interval & Duration	Adult Dose (max)	Pediatric Dose (max)	Criteria for Completion	Monitoring	Comments
INH	Daily for 9 mos	5 mg/kg (300 mg)	10-20 mg/kg (300 mg)	270 doses within 12 mos	Clinical monitoring monthly. Liver function tests[1] at baseline in selected cases[2] and repeat measurements if baseline tests are abnormal, patient is at high risk for adverse reactions, or patient has symptoms of hepatitis.	Preferred regimen for all persons. In HIV-infected patients, INH may be administered concurrently with NRTIs, protease inhibitors, or NNRTIs
	Twice-weekly for 9 mos	15 mg/kg (900 mg)	20-40 mg/kg (900 mg)	76 doses within 12 mos	**{tc ""}**	DOT must be used with twice-weekly dosing**{tc "DOT must be used with twice-weekly dosing"}**
INH	Daily for 6 mos	5 mg/kg (300 mg)	nr	180 doses within 9 mos		Alternate regimen for adults.
	Twice- weekly for 6 mos	15 mg/kg (900 mg)	nr	52 doses within 9 mos	**{tc ""}**	DOT must be used with twice-weekly dosing**{tc "DOT must be used with twice-weekly dosing"}**
RIF plus PZA	Daily for 2 mos	RIF 10mg/kg (600 mg) PZA 15-20 mg/kg (2.0 g)	nr	60 doses within 3 mos	Clinical monitoring at baseline, weeks 2, 4, 6 and 8. Liver function tests[1] at baseline and at 2, 4, and 6 weeks for all patients on this regimen.	Alternate regimen for adults. In HIV-infected patients, certain protease inhibitors or NNRTIs should not be administered concurrently with RIF; an alternative is rifabutin 300 mg daily. Preferred regimen for persons exposed to INH-resistant, RIF susceptible TB. RIF-PZA is not recommended for persons with underlying liver disease or for those who have had INH-associated liver injury. The 2-month RIF-PZA treatment regimen for LTBI should be used with caution, especially in patients concurrently taking other medications associated with liver injury, and those with alcoholism, even if alcohol use is discontinued during treatment. This regimen is not included in the list of accepted regimens of treatment for LTBI in children under age 18.
RIF	Daily for 4 – 6 mos.	10 mg/kg (600 mg)	10-20 mg/kg (600 mg)	120 doses within 6-8 mos	Clinical monthly monitoring Complete blood count, platelets, and liver function tests[1] at baseline in selected cases[2] and repeated measurements if baseline results are abnormal or patient has symptoms of adverse reactions	Alternate regimen for adults. For persons exposed to INH resistant, RIF susceptible TB and those who cannot tolerate PZA.
INH plus RIF	Daily for 4 mos.	INH 5 mg/kg (300 mg) RIF 10mg/kg (600 mg)		120 doses within 6 mos	See INH and RIF	Alternate regimen for TB Class 4 (history of previous TB or abnormal but stable radiographic findings without evidence of active TB.)

Abbreviations: INH = isoniazid, RIF = rifampin, PZA = pyrazinamide, NRTIs = nucleoside reverse transcriptase inhibitors, NNRTIs = non-nucleoside reverse transcriptase inhibitors, DOT = directly observed therapy, mos. = months, nr = not recommended

Pregnancy: INH regimens preferred for pregnant women. Some experts would use RIF plus PZA as an alternate regimen in HIV-infected pregnant women. PZA should be avoided during the first trimester.

MDR-TB exposure: For persons who are likely to be infected with INH and RIF (multi-drug) resistant TB and at high risk of reactivation, PZA and ethambutol or PZA and a fluoroquinolone are recommended depending on the sensitivities of the M. tb isolate. (Consult expert.)

[11] AST or ALT and serum bilirubin

[2] HIV Infection, history of liver disease, alcoholism, and pregnancy